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EXAMINER	
GREENE, JAIME M	
ART UNIT	PAPER NUMBER
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,661	PARK ET AL.	
	Examiner	Art Unit	
	JAIME M. GREENE	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/06, 5/06, 1/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to papers filed 12/19/07. Claims 7-9 are pending and are under examination on the merits.

Election/Restrictions

2. Applicant's election without traverse of Group II, claims 7-9, and SEQ ID NO:5, having the G allele at the polymorphic site position 101 is acknowledged.

3. It is noted that the subject matter of the nonelected inventions has been cancelled by Applicants.

Specification

4. A. The use of the trademarks MassEXTEND and Sequenom (e.g. pg 6) has been noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

B. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code – see, for example, page 11. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on, e.g., page 11. Applicant is required to delete

the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Priority

6. Acknowledgment is made of applicant's claim for foreign priority based on applications filed in Korea on 2/2/04 and 2/1805. It is noted, however, that a certified copy of each of the foreign applications has not been filed as required by 35 U.S.C. 119(b). It is also noted that a foreign document was filed 9/16/05, however there is no indication on that non-English document if it is a certified copy of one of the foreign priority documents.

Claim Rejections - 35 USC § 112

7. Claims 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 7 is indefinite because the claims do not recite a clear nexus between the preamble of the claims and the final step of the claims. The claim is drawn to a method for diagnosing colorectal cancer. However, claim 7 recites a final process step of determining a nucleotide present in the individual at a polymorphic site. The final process step does not detail how to diagnose colorectal cancer.

9. Claims 7 is further indefinite over parenthetical recitation of (position 101). Because the recitation is in parentheses it is not clear if this recitation is meant to be a

limitation to the claims. Further, it is entirely unclear what this arbitrary identifier means. It is noted that in the interest of compact prosecution, the recitation of (position 101) will be interpreted as "at position 101".

10. Claims 8 and 9 are indefinite for the reasons applied to claim 7.

11. The term "higher likelihood" in claim 9 is a relative term which renders the claim indefinite. The term "higher likelihood" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 112 Written Description

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 7-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 7-9 are broadly drawn to a method of diagnosing colorectal cancer in any individual, which comprises: isolating a nucleic acid sample from any individual and determining a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. Since the term “individual” is not defined, this broadly encompasses any organism.

Also, the method of claims 7 and 9 do not recite any steps for determining the a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. Therefore, the methods broadly encompass examining sequences in linkage disequilibrium with said polymorphic site. The method of claim 8, which recites a hybridization step, broadly reads on immobilizing any sequence comprising any 10 or more contiguous nucleotides of SEQ ID NO:5 along with any 11th nucleotide to an array and therefore does not require that the polymorphic site be within those 10 or more contiguous nucleotides.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the specification provides SEQ ID NO: 5. However, claims 7 and 9 broadly encompass examining SNPs in Linkage disequilibrium with a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 and therefore the definition is not considered representative of the genus of sequences that could be used to determine the nucleotide at polymorphic site of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. Claim 8 broadly encompasses any sequence that has at least 10 nucleotides of SEQ ID NO: 5 and that has an additional G or a T. Finally, Halushka (Halushka, et al. Nature Genetics, 1999; 22:239-247) teaches assessing the age or ancestral state of human SNP alleles by obtaining the corresponding orthologous sequence from the closely related great apes (page 244, column 1, paragraph 2), and Halushka teaches that the data suggest that 95% of population-specific SNPs arose in the human lineage after

population differentiation and that the common allele [between human and ape] is the likely ancestral state. This suggests that SNPs are not common between organisms and since the specification does not provide any sequence data for non-human organisms, the sequences provided are not considered representative of corresponding SNPs in non-human organisms.

Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than by name and functional characteristics), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the specification provides SEQ ID NO:5. However, for claims 7 and 9, the specification does not provide any structural information to identify sequences in linkage disequilibrium with a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. For claim 8, For claim 8, the claim broadly encompasses any sequence that has at least 10 nucleotides of SEQ ID NO: 5 and that has an additional G or T nucleotide, which could encompass a wide range of sequences including variant, mutations, and sequences from other genes or chromosomes. However, the specification does not provide guidance outside of SEQ ID NO:5 for identifying such sequences. Further, the specification does not provide any guidance for identifying corresponding SNPs in non-human organisms.

Applicants' attention is directed to the decision in In re Shokal, 113 USPQ 283 (CCPA 1957) wherein is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

Also, Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

In the instant application, since the specification does not provide sequence or structural guidance for 1) sequences in linkage disequilibrium with a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5, 2) the large variety of sequences that are encompasses by the recitation of at least 10 contiguous nucleotides of SEQ ID NO:5 and a nucleotide at position 101 of SEQ ID NO:5 or 3) corresponding non-human SNPs, while the skilled artisan can identify the detailed

structure of a nucleotide at polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 in humans, one of skill in the art cannot envision the detailed structure of 1) a nucleotide at polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 in any individual, 2) at least 10 contiguous nucleotides of SEQ ID NO:5 and a nucleotide at position 101 of SEQ ID NO:5 in any individual, or 3)sequences used to determine a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 in any individual.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as

by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The lack of information regarding 1) a nucleotide at polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 in any individual, 2) at least 10 contiguous nucleotides of SEQ ID NO:5 and a nucleotide at position 101 of SEQ ID NO:5 in any individual, or 3) sequences used to determine a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 in any individual is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of a method of diagnosing colorectal cancer in any individual, which comprises: isolating a nucleic acid sample from any individual and determining a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for claims 7-9.

Claim Rejections - 35 USC § 112 Enablement

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 7-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing colorectal cancer in a Korean human individual, which comprises: isolating a nucleic acid sample from a Korean human individual, amplifying the sequence of SEQ ID NO: 5 by PCR, hybridizing primers to the amplified DNA, adding a polymerization solution that contains a sequence terminating ddTTP and allowing an extension reaction to proceed, determining the sequence of the products by mass spectrometry in order to determine if the sequence contains a G as the polymorphic site of position 101 in SEQ ID NO: 5, wherein when a G is present it is determined that the patient has or will develop colorectal cancer, does not reasonably provide enablement for a method of diagnosing colorectal cancer in any individual, which comprises: isolating a nucleic acid sample from any individual and determining a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Teletronics Inc*, 8 USPQ2d 1217 (Fed Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte*

Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986)) and *In re Wands* 8 USPQ2d 1400 (Fed. Cir. 1988)).

The breadth of the claims and nature of the invention

Claims 7-9 are broadly drawn to a method of diagnosing colorectal cancer in any individual, which comprises: isolating a nucleic acid sample from any individual and determining a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. Claim 9 further requires that the nucleotide is a G. Since the term "individual" is not defined, this broadly encompasses any organism. Also, the method of claims 7 and 9 do not recite any steps for determining the a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. The method of claim 8, which recites a hybridization step, broadly reads on hybridizing any 10 or more contiguous nucleotides of SEQ ID NO:5 to an array and therefore does not require that the polymorphic site be within those 10 or more contiguous nucleotides. Therefore, the methods broadly encompass examining sequences in linkage disequilibrium with said polymorphic site.

Guidance in the Specification and Working Examples

The specification teaches studying an association between the position 101 polymorphism in SEQ ID NO: 5 and colorectal cancer (pg 4). The specification teaches performing DNA nucleotide sequence analysis on blood collected from Korean colorectal cancer patients and normal persons (pg 4). The specification teaches in Table 1 that the G allele has an odds ratio of 1.52, a confidence interval of 1.182 and 1.961 and a chi-square value of 4.62×10^{-3}. The specification teaches in example 1 that

the patients were 300 Korean colorectal cancer patients and 300 Korean controls (see page 11). Therefore, while this indicates that the G allele of SEQ ID NO: 5 may be associated with colorectal cancer in a Korean patient population, there is no indication in the specification that the data can be extrapolated to other patient populations.

Claim 7 broadly reads on the presence of any nucleotide at position 101, however the specification does not provide data for the presence of an A or a G at said position. The specification also does not teach linkage disequilibrium studies, and the specification does not teach any studies in organisms other than humans. Claim 8 broadly reads on a method using 10 or more contiguous nucleotides of SEQ ID NO: 5 plus a G or T nucleotide and therefore reads on identifying sequences in other genes or on other chromosomes that are unrelated to the identification of the polymorphism of SEQ ID NO: 5.

The unpredictability of the art, the state of the prior art, level of skill in the art

While the state of the art and level of skill in the art with regard to correlating polymorphisms with disease state is high, the level of unpredictability in associating any polymorphism with a particular disease state is even higher. The level of unpredictability is demonstrated by the prior art, the post filing art, and the instant specification.

Regarding using polymorphisms to make predictions, the art teaches genetic variations and associations are often irreproducible. Hirschhorn (Hirschhorn et al. Genetics in Medicine. Vol. 4, No. 2, pages 45-61, March 2002) teaches that most reported associations are not robust. Of the 166 associations studied three or more

times, only 6 have been consistently replicated. Hirschhorn suggests a number of reasons for the irreproducibility of studies, suggesting population stratification, linkage disequilibrium, gene-gene or gene-environment interactions, and weak genetic effects and lack of power are possible factors that lead to such irreproducibility. Hirschhorn et al. caution that the current irreproducibility of most association studies should raise a cautionary alarm when considering their use as diagnostics and prognostics (p. 60, Col. 2). Thus, Hirschhorn cautions in drawing conclusions from a single report of an association between a genetic variant and disease susceptibility.

Regarding linkage disequilibrium studies, Long (Long, et al. BMC Genet. 2004 May 24;5:11) teaches performing a study to determine the Linkage Disequilibrium and haplotype characteristics in eight candidate genes for the two common complex disorders, osteoporosis and obesity (pg 2, col 1). Long teaches that LD was inferred either by using unrelated random sample or family data and that the LD values evaluated from these two different data sets were correlated, but in some instances they were quite different(pg 4, col 2). Long teaches that family subjects contain more information than unrelated random individuals, and the inference of LD using family data is more accurate (pg 4, col 2). Long teaches that sample size is another important factor influencing the accuracy of LD evaluation with larger sample sizes minimizing sampling error and producing more accurate evaluation of LD (pg 4, col 2 to pg 5, col 1). Long also teaches several limitations of the study including that while using a 15-kb chromosome-wide resolution for LD pattern and haplotype structure study is acceptable, it is not ideal, and that the study was restricted to Caucasians of European descent,

which limits the ability to perform cross-population comparisons, because genetic diversity and LD extent differ between populations (pg 5, col 2).

Regarding polymorphisms in non-human organisms, Halushka (Halushka, et al. Nature Genetics, 1999; 22:239-247) teaches assessing the age or ancestral state of human SNP alleles by obtaining the corresponding orthologous sequence from the closely related great apes (page 244, column 1, paragraph 2). Halushka teaches that although there was a high degree of sequence identity between great ape and human samples (page 244, column 2, paragraph 1), the average nucleotide divergence between human and chimpanzee, gorilla and orangutan was 0.010, 0.012 and 0.021, respectively, and that and that these values are more than ten times greater than the within-population human diversity (page 244, column 2, paragraph 1). Halushka teaches that the data suggest that 95% of population-specific SNPs arose in the human lineage after population differentiation and that the common allele [between human and ape] is the likely ancestral state.

Quantity of Experimentation

Claims 7-9 are broadly drawn to a method of diagnosing colorectal cancer in any individual, which comprises: isolating a nucleic acid sample from any individual and determining a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. The specification only teaches the polymorphism at position 101 within a polynucleotide of SEQ ID NO:5, and the specification teaches an association between the G allele and colorectal cancer, however the specification also presents conflicting data regarding the make-up of the patient population studied. For claim 7, the claims

read on the presence of any polymorphism being present at the identified location (because the claim requires a nucleotide at the site position 101 but does not require it be the nucleotide in the sequence of SEQ ID NO:5), however the specification only teaches studying the G and T alleles. For claim 8, the claim broadly encompasses any sequence that has at least 10 nucleotides of SEQ ID NO: 5 and that has an additional G or T nucleotide, which could encompass a wide range of sequences including variant, mutations, and sequences from other genes or chromosomes. Hirschhorn teaches that most reported genetic associations are not robust and suggests population stratification, linkage disequilibrium, gene-gene or gene-environment interactions, and weak genetic effects and lack of power are possible factors that lead to such irreproducibility. Therefore, the skilled artisan would be required to perform a large study to determine if the G allele is predictive of colorectal cancer in any population. Further, regarding claim 7, the skilled artisan would be required to perform a large study to determine if the presence of an A or C at the polymorphic site can be associated with colorectal cancer, and regarding claim 8, the skilled artisan would be required to perform a large study to determine if all the possible sequences encompassed by the claim are associated with colorectal cancer. This would require undue and unpredictable experimentation with no expectation of success.

Claims 7 and 9 are broadly drawn to a method of diagnosing colorectal cancer in any individual, which comprises: isolating a nucleic acid sample from any individual and determining a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5. Because the claims only requiring determining a nucleotide of polymorphic

site (position 101) within polynucleotide of SEQ ID NO:5, the claims broadly read on not just sequencing methods but also other methods of identifying the presence or absence of a polymorphism such as linkage disequilibrium. The specification only teaches identifying the polymorphism by sequencing the polymorphic site, and the specification conflicts on the identify of the patient population with pg 4 suggesting that the patients were from a general population but pg 11 suggesting that the patients were Korean. Long teaches that the accuracy of linkage disequilibrium studies depends on whether the patient population is comprised of families, and Long teaches that in order to extend the results of LD studies to the general population, data should be collected from a variety of ethnic groups. Therefore, the skilled artisan would be required to perform, e.g. a large LD study using patient data from a large number of families from a variety of ethnic groups in order to use the results to determine if any other SNPs can be used to determine a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 in order to make predictions about colorectal cancer. This would require undue and unpredictable experimentation with no expectation of success.

Claims 7-9 are broadly drawn to a method of diagnosing colorectal cancer in any individual. Since the specification does not define individual, this broadly encompasses any organism. However, the specification only teaches studies in humans. Halushka teaches assessing the age or ancestral state of human SNP alleles by obtaining the corresponding orthologous sequence from the closely related great apes, and Halushka teaches that the data suggest that 95% of population-specific SNPs arose in the human lineage after population differentiation and that the common allele [between human and

ape is the likely ancestral state, suggesting that SNPs are not common between organisms. Therefore, the skilled artisan would be required to perform a large study in order to identify any corresponding SNPs in non-human organisms and then determine of if those SNPs could be used to diagnose colorectal cancer. This would require undue and unpredictable experimentation with no expectation of success.

Claims 9 is broadly drawn to a method of diagnosing colorectal cancer in any individual, which comprises: isolating a nucleic acid sample from any individual and determining a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5, wherein when the determined nucleotide is G , it is determined that the individual has a higher likelihood of being diagnoses as at risk of developing colorectal cancer. The specification suggests a significant correlation between a G nucleotide of polymorphic site (position 101) within SEQ ID NO:5 and colorectal cancer, however the specification does not teach a scale for determining the likelihood of being diagnosed as a colorectal cancer patient or as at risk of developing colon cancer. Therefore the skilled artisan would need to perform undue and unpredictable experimentation in order to determine a scale for estimating the likelihood of being diagnosed as a colorectal cancer patient or as at risk of developing colon cancer.

Conclusion

Given the lack of data from all organisms, the lack of details on how to determine a nucleotide of polymorphic site (position 101) within SEQ ID NO:5, and the lack of information on how to determine the likelihood of being diagnosed as at risk of developing colon cancer, a method of diagnosing colorectal cancer in any individual,

which comprises: isolating a nucleic acid sample from any individual and determining a nucleotide of polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 is replete with unpredictable experimentation that is considered undue.

Thus given the broad claims in an art whose nature is unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the methods of the claims as broadly written.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claim 7 is rejected under 35 U.S.C. 102(e) as being anticipated by Wang (Wang, US PGPub 20050228172, published 10/13/05, filed 8/8/01).

Regarding claim 7, Wang teaches that genomic DNA was isolated from a plurality of human individuals (pg 4, para 34). Wang teaches that the DNA was sequenced to identify SNPs (pg 4, paras 35-36). Wang teaches that the SNPs identified are in Figure 2 (pg 4, para 36) and the caption for Figure 2 (pg 1, para 13) teaches that the Figure includes all of the SEQ ID NOs and the SNPs identified for each one. In addition the sequence listing from the identified website (pg 5, sequence listing)

includes SEQ ID NO: 209468, which aligns with 100% of instant SEQ ID NO: 5 (see alignment below).

By isolating DNA from humans and determining the sequence SEQ ID NO: 209468, Wang teaches all of the active step of claim 7.

Also, s noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." Further, in Pitney Bowes Inc. v. Hewlett-Packard Co., 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation". In the present situation, the claim language of "a method of diagnosing colorectal cancer in an individual" is a statement of purpose and intended result and does result in a manipulative difference in the method steps of the claims. Accordingly, the process steps are able to stand alone and therefore the preamble limitation is not accorded patentable weight.

Therefore all limitations of claim 7 have been taught by the reference.

Alignment

Alignment between instant SEQ ID NO: 5 (Query) and SEQ ID NO: 209468 from Wang (Db)

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Qy 1   CCCAGGATTGGAAATGATGGATGCTTTCCAGGGGCCCCGATCCATCATCAGATGAATACG 60
       ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db134  CCCAGGATTGGAAATGATGGATGCTTTCCAGGGGCCCCGATCCATCATCAGATGAATACG 193

Qy 61  CAGCCCCCTCCCCAAGGAAGCTCCTGGTTCATTGAGATGCNTAATTCTCTCCTTATTTTC 120
       ||||||||||||||||||||||||||||||||||||:||||||||||||||||||||||
Db194  CAGCCCCCTCCCCAAGGAAGCTCCTGGTTCATTGAGATGCKTAATTCTCTCCTTATTTTC 253

Qy121  ATTACTGTTTCTCGTTTGTATGGATTATTTTTCTTCAGTAATCTGGGCTTTACATGACTG 180
       ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db254  ATTACTGTTTCTCGTTTGTATGGATTATTTTTCTTCAGTAATCTGGGCTTTACATGACTG 313

Qy181  AATAAGAAAATCATTTGTTCA 201
       |||||||||||||||||||||
Db314  AATAAGAAAATCATTTGTTCA 334
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Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (Wang, US PGPub 20050228172, published 10/13/05, filed 8/8/01).

It is noted that the preamble of claim 7 recites an intended use and therefore does not carry any patentable weight for purposes of this rejection.

Regarding claim 7, Wang teaches that genomic DNA was isolated from a plurality of human individuals (pg 4, para 34). Wang teaches that the DNA was sequenced to identify SNPs (pg 4, paras 35-36). Wang teaches that the SNPs identified are in Figure 2 (pg 4, para 36) and the caption for Figure 2 (pg 1, para 13) teaches that the Figure includes all of the SEQ ID NOs and the SNPs identified for each

one. In addition the sequence listing from the identified website (pg 5, sequence listing) includes SEQ ID NO: 209468, which aligns with 100% of instant SEQ ID NO: 5 (see alignment above).

By isolating DNA from humans and determining the sequence SEQ ID NO: 209468, Wang teaches all of the active step of claim 7.

Regarding claim 8, Wang teaches that oligonucleotides that recognize one allele of a SNP nucleic acid, or preferably at least 10 SNP nucleic acids, are immobilized on a filter, that PCR-amplified DNA made from a sample of blood from an individual is hybridized to the array, and that the hybridization results are detected (pg 4, para 41).

While Wang does not specifically state that a polynucleotide containing 10 nucleic acids of SEQ ID NO:5 and the nucleotide at position 101 is immobilized, it would have been prima facie obvious to the ordinary artisan to use a probe of 11 nucleic acids including the SNP site of SEQ ID NO: 209468 from Wang to genotype a human sample because such methods of generating SNP probes for microarrays are common practice in the art. Further, Wang clearly contemplates using the identified SNP sequences to create microarrays for genotyping an individual, and therefore, Wang renders the method of claim 8 obvious.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

21. Claims 7-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-10 of copending Application No. 11451665. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 7-10 are methods of diagnosing colorectal cancer using a polymorphism that corresponds to position 101 in a polynucleotide sequence of SEQ ID NO: 1 or 2. Since the specification does not define "corresponds to" the claims are broadly drawn to identifying any polymorphism. Therefore, it would have been prima facie obvious to the ordinary artisan to identify any polymorphism, e.g. associated with colorectal cancer, including a nucleotide of polymorphic site (position 101) within polynucleotides of SEQ ID NO: 5 of instant claims 7-9, which are broadly encompassed by the recitation in claims 7-10 of '665 of a polymorphism that corresponds to position 101 in a polynucleotide sequence of SEQ ID NO: 1 or 2.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

None of the claims have been allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAIME M. GREENE whose telephone number is (571)270-3052. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jaime M. Greene 2/26/08

/Carla Myers/
Primary Examiner, Art Unit 1634